Assessment of Dry Socket after Mandibular Third Molar Surgery Using Platelet-Rich Fibrin - A Prospective Clinical Study

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ABSTRACT

Objective: To determine the efficacy of Platelet-Rich Fibrin (PRF) in preventing Dry Socket (DS) after mandibular third molar surgery in comparison with the control group.

Study Design: Experimental study.

Place and Duration of the Study: Oral and Maxillofacial Surgery Department, Dental Section, Faisalabad Medical University, Faisalabad, Pakistan, from July 2019 to June 2021.

Methodology: Patients aged 18-35 years with good oral hygiene, and requiring surgical extraction of their mandibular third molar were included in the study. Those with periodontal disease, pregnant or nursing women, smokers, or allergic to the agents that were recommended for use before and after surgery, were excluded. Patients presenting for surgical removal of the mandibular third molar and meeting the inclusion criteria were enrolled and randomly divided into 2 groups. Standard protocol for tooth removal was followed in both groups. Group1 (study group) received PRF and group 2 (control group) did not receive PRF.

Results: A total of 170 consecutive patients (85/group) were randomly selected and allocated to the study group and control group. The mean age in the study group was 24.28±3.7 years while the mean age in the control group was 24.14±3.64 years. Out of them, 51.2% (n=87) were males and 48.8% (n=83) were females with a M: F of 1:1.05. On the 3rd postoperative day, DS frequency in the study group was 2.4% (n=2) and 18.8% (n=16) in the control group (p=0.0001), which reduced to 01 and 05 respectively on 7th day (p=0.096).

Conclusion: PRF administration was effective in preventing DS on the third postoperative day in mandibular third molar - surgery, with statistically significant results. However, on postoperative day 7, the results were not statistically significant.

Key Words: *Third molar, Tooth extraction, Dry socket, PRF.*

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INTRODUCTION

Extraction of the impacted mandibular third molar is one of the common oral surgical procedures performed in oral surgery.[1,2] This procedure can be associated with significant postoperative complications such as pain, trismus, oedema, postoperative wound infection, and dry socket (DS).[2,3] DS is a post-extraction complication that presents with pain, increasing in intensity from 1st to 3rd postoperative day; exhibits an empty alveolar socket that is not covered by a blood clot or healing epithelium and exists inside or around the socket for 3 to 7 days after the extraction procedure.[3]

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It is one of the most common complications after the mandibular 3rd molar extraction with an average incidence of about 3-45%.[1-3] The incidence of DS is higher in the 3rd and 4th decades of life and is more prevalent in females (F:M=5:1).[3] The main pathophysiologic factor of DS is localised fibrinolysis resulting in the disintegration of blood clot.[2,3] Other predisposing factors include surgical trauma, increased bone density, the difficulty of surgery, use of oral contraceptives, smoking, alcohol intake, poor oral hygiene, physical dislodgement of the blood clot, and previously existing bacterial infection.[1-7]

Many interventions for the prevention of DS have been used over the years including topical chlorhexidine, systemic antibiotics, socket lavage, anti-fibrinolytic agents, and packing of medicaments (like eugenol, chlorhexidine, *etc*.) into the socket during surgery but the results remain elusive.[4-6] Platelet-Rich Plasma (PRP) gave promising results but was not used widely due to the very complex preparation protocol.[7-9] In contrast, Platelet-Rich Fibrin (PRF) is a second-generation platelet concentrate with several advantages over PRP; such

as ease of preparation and lack of biochemical manipulation of blood; which makes this preparation strictly autogenous.[9-11]

The PRF is a middle layer of autologous blood between the upper straw-coloured, acellular plasma layer and lower, red-colored RBC fraction;[1] was obtained after centrifugation of blood at 3000 RPM for 10 minutes.[3,9] It is a platelet concentrate that contains about 65% the leukocytes, the highest values of platelets, cytokines, PDGF, VEGF, TGF beta, EGF[12-14] *etc*. It can stimulate osteogenesis and provides epithelial coverage consisting of fibrin in addition to revascularisation. In some international studies, the incidence of DS without PRF is 9.5% while with PRF 1% has been reported in recent years.[15]

As no definite option exists which can reliably prevent DS, therefore, the rationale behind this study was to look for a reliable method in the form of PRF for the prevention of DS after mandibular 3rd molar extraction. The objective of this study was to determine the efficacy of Platelet-Rich Fibrin (PRF) in preventing dry socket (DS) after mandibular third molar surgery in comparison with the control group.

METHODOLOGY

This prospective comparative experimental study was conducted in the Oral and Maxillofacial Surgery Department, Dental Section, Faisalabad Medical University, from July 2019 to June 2021. Ethical approval was obtained from the Institutional Ethical Review Committee before study initiation [Ref.No. FMUF 10-04-2019-IRB-0006912 (OHRP, USA)]. A total of 170 patients, who met the inclusion criteria, were included in the study through OPD using consecutive non-probability sampling techniques. The sample size was calculated using the WHO calculator with a 95% confidence interval, study power of 80%, and expected incidence of DS as 9.5% without PRF and 1% with PRF.

The inclusion criteria were all the patients aged 18-35 years, irrespective of gender, requiring surgical extraction of the mandibular third molar and willing to cooperate with the study protocol. Patients with any comorbid condition or contraindications to surgery *e.g* diabetes mellitus, hypertension, pregnancy, acute pericoronitis of mandibular 3rd molar 20 with/without trismus, smokers and female patients using oral contraceptives were excluded from the study. Preoperative medical records were completed including chief complaint, medical and dental history, oral hygiene assessment, panoramic radiographs, and baseline blood investigations (including complete blood count, bleeding profile, and viral hepatitis screening). The procedure was explained to the patients and written informed consent was obtained. All included patients were randomly divided into two groups *i.e*. the study group and the control group using the coin-toss method. PGR level-II and above operator performed a standardised surgical procedure for all the patients using a strict aseptic technique and local anaesthesia. If necessary, bone removal and tooth sectioning techniques were performed using a slow-speed handpiece while irrigating with a copious amount of normal saline. After tooth extraction, the PRF clot was prepared using Choukroun's method.[12-15] 10 ml of venous blood was withdrawn from the patient's cubital fossa and was collected in the two 5ml vacutainers blood collection tubes without anticoagulant and was immediately centrifuged at 3000 rpm for 10 minutes. Blood was separated into three layers after centrifugation *i.e*. the middle layer containing the PRF was collected.[12-15] Collected PRF was placed into the extraction socket of patients included in the study group, but no such material was placed in the control group. The soft tissue mucoperiosteal flap was approximated with black silk 3-0. Identical postoperative instructions with special emphasis on avoidance of spitting along with oral hygiene maintenance and medications were given to all patients postoperatively. Postoperative medications included Tab. Amoxicillin 500mg + Clavulanic acid 125 mg TDS, and Tab. Ibuprofen 400mg TDS for 05 days. Follow-up visits were on the 3rd and 7th postoperative days for evaluation of DS. DS was labelled as 'yes' or 'no' based on the presence or absence of two parameters *i.e* pain and empty socket. The pain was observed on the standard visual analog scale (VAS). A blinded observer evaluated pain on the 3rd and 7th postoperative days to reduce bias. The pain was labelled as 'yes' if the patients reported the presence of persistent, throbbing postoperative pain inside and in the perimeter of the empty alveolar socket that is not adequately alleviated by analgesics (pain score on VAS >3) and 'no' if the pain score was ≤3 on VAS. The empty socket was analysed clinically by observing soft tissue healing covering the walls of the socket. The empty socket was labelled as 'yes' if there was the partial or complete loss of blood clot on the 3rd and 7th day with exposed socket walls while it was labelled as 'no' if the extraction socket was covered with healthy soft pink granulation tissue covering the walls of the socket with no socket wall exposed. PRF was categorised as effective in preventing DS based on the presence or absence of both these two parameters *i.e.* pain and empty socket outcome was 'no' on the 3rd and 7th postoperative day. Sutures were removed on the 7th postoperative day. If a patient failed to report for follow-up on the 3rd and 7th postoperative days, he/she was removed from the study, and the next patient was enrolled. DS, when found, was treated by irrigation with normal saline, packing of the extraction socket with an obtundent dressing and simple analgesics.

Data were entered and analysed by using SPSS version 16. Mean and standard deviation (SD) were calculated for quantitative variables such as age. Frequencies and percentages were calculated for qualitative variables such as gender, pain, empty socket, and DS. A chi-square test was used to compare DS between two groups (efficacy), and a p-value ≤0.05 was taken as statistically significant. Effect modifiers such as age and gender were controlled by stratification. A post-stratification chi-square test was applied.

RESULTS

Among the total of 170 participants (85 in each group), the mean age in the study group was 24.28±3.7 years while the mean age in the control group was 24.14±3.64 years.

Table I: Dry socket at 3rd and 7th postoperative day.

Outcome	Group		Total	p-value
	Study group	Control group		
The dry socket on the 3rd postoperative day				
Yes	2 (2.4%)	16 (18.8%)	18 (10.6%)	0.0001
No (Efficacy)	83 (97.6%)	69 (81.2%)	152 (89.4%)	
Total	85	85	170	
The dry socket on the 7th postoperative day				
Yes	1 (1.2%)	5 (5.9%)	6 (3.5%)	0.096
No (Efficacy)	84 (98.8%)	80 (94.1%)	164 (96.5%)	
Total	85	85	170	

Chi-square test was applied.

Regarding gender distribution, 51.2% (n = 87) were males and 48.8% (n = 83) were females with a M: F of 1:1.05. On the 3rd postoperative day, DS frequency in the study group was 2.4% (n = 2) while in the control group was 18.8% (n = 16) and showed a statistically significant difference (p-value = 0.0001). However, on the 7th postoperative day, DS frequency in the study group was 1.2% (n = 1) while in the control group was 5.9% (n = 5) and showed a statistically insignificant difference (p-value = 0.096) as shown in Table I.

DISCUSSION

DS is a relatively common and painful complication requiring intervention for treatment. About 45% average incidence of DS after mandibular third molar extraction has been reported in the previous literature. DS is a multi-factorial condition. In any case, all the factors contributing to DS, eventually fail the maturation of the originally formed blood clot.[2,3] Various materials have been investigated extensively to prevent DS. Out of all of them, autologous materials made from a patient's blood contain a concentrate of a significant number of the factors required for typical wound healing and are always more promising.

As an autologous material, platelet concentration have become an important component of routine oral surgery[9-15] and promote tissue regeneration.[12-14] One of the platelet concentrates is PRF. It is a natural fibrin-based biomaterial characterised by slow polymerisation during its manufacturing. It enhances angiogenesis, acts as a guide for epithelium migration, supports immunity, protects open wounds by covering damaged tissue through beneficial effects on epithelial cells and fibroblasts, and promotes - wound healing.[12-14] Retention of PRF clots is thought to lead to decreased DS due to the effects of fibrin matrix and - platelet degranulation. It is a reservoir of platelets, white blood cells, cytokines, and immune cells. Upon degranulation, it allows the sustained release of cytokines from alpha granules of platelets such as TGFb-1 (transforming growth factor-beta), PDGF (platelet-derived growth factor), VEGF (vascular endothelial growth factor) and EGF (epithelial growth factor). TGFb-1 is a morphogen that can promote osseous tissue activity; PDGF regulates the migration and proliferation of mesenchymal cells near the extraction site to stimulate osseous, endothelial, and fibroblastic proliferation; VEGF and EGF aid in the proliferation and differentiation of various cell types. The physical displacement of erythrocytes from the alveolar socket by placing PRF also explains the healing capacity of the alveolus. Using PRF as prophylaxis for DS formation showed a 90% reduction in the DS incidence in patients where PRF was placed at the surgical site of the mandibular 3rd molar.[15] PRF is a healing biomaterial and perhaps this could explain the significant difference in the incidence of DS occurring in the PRF group compared to the control group.[15-24]

Out of the total of 170 patients, incidence of DS at the third postoperative day was found in 18 (10.6%) patients out of which 2 (2.4%) were in the study group and 16 (18.8%) were in the control group. The occurrence of DS was less in the patients who received PRF with a statistically significant p-value of 0.0001 on the third postoperative day. This is in agreement with other studies broadly in terms of reduction in the incidence of DS with PRF use.[3-5,12,17] However, the reduction rates varied. In this study, the frequency of DS was 2.4% (2 sites out of 85) with PRF placement and 18.8% (16 sites out of 85) without PRF. Hoaglin *et al.* reported 1% (2 sites out of 200)[15] with PRF placement and 9.5% (19 of 200 sites) without PRF. This difference may be due to different working conditions, patient's oral hygiene, diet pattern & patient's precautionary measures taken postoperatively. However, both studies are in agreement concerning the significant reduction in the occurrence of DS with the use of PRF. The present study showed a 97.6% reduction whereas Hoaglin *et al*. found a 90% in reduction DS with the use of PRF. This difference may be due to different working conditions, patient oral hygiene, dietary patterns, and patient postoperative precautions. However, both studies are in agreement that PRF use significantly reduces the incidence of DS.

DS was found in 6 (3.5%) patients on the 7th postoperative day, out of which 1 (1.2%) was in the study group and 5 (5.9%) were in the control group. This may be because measures for pain would have been taken by the patient, and to some degree, resolution of DS would have taken place till the 7th postoperative day.

Regarding age, the mean ages of the patients in the previous studies were 24-25 and 23-24 years,[4,7,10,13,14] whereas in this

study the mean age was 24.28±3.7 years in the study group and (24.14±3.64) in the control group, in accordance with the previous studies. These results are consistent with the previous studies in which DS is more prevalent in patients >25 years and without the use of PRF.[4,7,10,13,14] This may be due to age-related slowing metabolism, delayed healing, and a weakened immune system. Surgical removal of the mandibular third molar is recommended before the age of 24 years. The results of the present study agree with the suggestions along with the use of PRF in patients presented >25 years of age.

Regarding gender, the results were in agreement with the previous literature.[14,21,23] It suggests that DS is more prevalent in females and without the use of PRF. This may be due to their use of oral contraceptives and the effect of estrogen on fibrinolysis.

PRF was easy to use, highly cost-effective from an application point of view and reduced the clinical time required to treat DS, all of these favour the standard use of PRF during surgical extraction of the mandibular third molar. This prophylactic technique also uses an autologous (derived from the patient's blood), a soluble biomaterial that does not introduce foreign material into the surgical site, thus preventing inflammatory foreign body reactions. However, quick blood processing is a critical factor in the success of that processing. Improper handling of blood samples quickly can result in diffusion and polymerization of fibrin within the glass tube, resulting in small, inconsistent clots. Some of the drawbacks of this technique in comparison to the conventional method of third molar surgery are the need for a centrifuge machine, additional prick for drawing blood and extra time required to process the blood, *etc*. However, the advantage of the prevention of DS outweighs these disadvantages as management of established DS would require more time and cost.

This study is based on the subjective VAS, the reduction in pain, although statistically significant, in the first few days after surgery should be noted with caution since pain sensation varies from patient to patient. The main limitations of the current study were the smaller sample size, shorter follow-up, and non-blinded study. With a similar degree of difficulty of extraction of mandibular 3rd molar, a larger sample size; a longer follow-up of each patient, and a double-blind split-mouth study are recommended for further evaluation. This is the only clinical study that compared the role of PRF in the prevention of DS among the Pakistani population to the best of the authors' knowledge.

The use of PRF to prevent DS in mandibular third molar extraction sockets is strongly recommended, especially when there are risk factors contributing to the formation of DS. Recommendations that could be made based on the results of such a study include the use of PRF as an effective treatment for DS, and the inclusion of PRF as a routine adjunctive therapy for patients undergoing mandibular third molar surgery.

However, additional multicenter studies are needed to overcome the limitations of this study before routine use in extraction sockets. Limitations of such a study would include the small sample size of patients, which would make it difficult to generalize the findings to a larger population. Additionally, the study may not account for other factors that could affect healing and recovery, such as patient's overall health, smoking status, and oral hygiene habits.

CONCLUSION

PRF administration was effective in preventing DS on the third postoperative day in mandibular third molar surgery, with statistically significant results. However, on postoperative day 7, the results were not statistically significant.

ETHICAL APPROVAL:
Ethical approval was obtained from the Institutional Ethical Review Committee before study initiation [Ref. No. FMUF 10-04-2019-IRB-0006912 (OHRP, USA)].

PATIENTS' CONSENT:
The procedure was explained to the patients and written informed consent was obtained.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
NI: Design of work, acquisition, analysis, and interpretation of data.
MUK: Critical analysis.
OSJ: Conception of work and critical revision.
KJZ: Literature search and appropriate investigation.
MMU: Data collection and drafting of the manuscript.
All the authors have approved the final version of the manuscript to be published.

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